REMARKS

Reconsideration and withdrawal of the rejections of this application and consideration and entry of this paper are respectfully requested in view of the herein remarks and accompanying information, which place the application in condition for allowance.

I. STATUS OF CLAIMS AND FORMAL MATTERS

Claims 1-34 are pending. Claims 3-6 and 8-12 are amended; claims 19-34 are added.

No new matter is added. Support for the amended claims is found throughout the specification.

It is submitted that these claims are patentably distinct from the references cited by the Examiner, and that these claims are in full compliance with the requirements of 35 U.S.C. §112. The amendments of the claims herein are not made for the purpose of patentability within the meaning of 35 U.S.C. §§ 101, 102, 103 or 112; but rather the amendments are made simply for clarification and to round out the scope of protection to which Applicants are entitled. Furthermore, it is explicitly stated that the herewith amendments should not give rise to any estoppel, as the herewith amendments are not narrowing amendments.

II. RESTRICTION REQUIREMENT

The Office Action required restriction from among:

I. Claims 1-12, drawn to a method for producing a lymphocyte or APC having tolerance to an allergen or antigen, comprising incubating a lymphocyte or APC with a composition capable of upregulating expression of an endogenous Notch or Notch ligand and the allergen or antigen, classified in class 435, subclass 325.

II. Claims 13-16, drawn to use of a composition capable of upregulating expression of an endogenous Notch or Notch ligand in an APC or lymphocyte in a method of producing regulatory lymphocytes capable of suppressing the activity of other lymphocytes, classified in class 435, subclass 7.24.

III. Claim 17, drawn to a method of treating a patient suffering from a disease characterized by inappropriate lymphocyte activity comprising administering a lymphocyte produced by methods of Group I, classified in class 424, subclass 184.1.

IV. Claim 18, drawn to a method for producing a lymphocyte having tolerance to an allergen or antigen comprising incubating an APC with a lymphocyte, classified in class 435, subclass 325.

Group I, claims 1-12, is elected with traverse. It is requested that new claims 19-34 be examined with the Group I claims, as they comprise elected subject matter. Applicants retain the right to file divisional applications to non-elected subject matter. Reconsideration and withdrawal of the restriction requirement are respectfully requested in view of the remarks herewith.

The present claims represent a web of knowledge and continuity of effort that merits examination in a single application. Indeed, the claims of all groups are related because they are all drawn to methods for preparing antigen presenting cells (APC) and lymphocytes that can suppress the activity of immune cells, and the use of compositions that upregulate Notch or Notch ligand in these methods.

In this regard, the Examiner's attention is respectfully directed to MPEP § 808.02 which states, ". . . restriction is not required unless one of the following reasons appears:

1. Separate classification;
2. Separate status in the art; or
3. Different field of search . . ."

Contrary to the guideline provided by the MPEP, Groups I, II and IV are in the same class, with Groups I and IV in the same subclass. Further, there is no evidence presented in the Office Action to demonstrate that the claims of the three Groups have acquired separate status in the art. Importantly, the claims in all four Groups involve the upregulation of the expression of endogenous Notch or Notch ligands in APC or lymphocytes, thereby encompassing the same field of search. Thus, restriction is not appropriate.

Additionally, the Examiner's attention is further directed to the text of MPEP § 803 which in part states:

> If the search and examination of an entire application can be made without serious burden, the Examiner must examine it on the merits ...

A search of the Group I claims will necessarily involve a search of the non-elected groups, particularly Group IV, which is classified in the same class and sub-class, and should therefore be rejoined to elected Group I.

The Office Action also required the election of a specific Notch or Notch ligand. Delta is elected with traverse. It is respectfully submitted that there is no basis for a restriction of this nature, since neither Notch nor Notch ligand is necessarily required in the claimed methods. The invention relates to use of a composition that is capable of upregulating expression of a Notch or Notch ligand. Since such a composition could affect the activity of any Notch or Notch ligand, is submitted that the upregulation of Delta, for example, would not be patentably distinct from the upregulation of Serrate if the activity is being modulated by the same composition.

The Office Action also required the election of a specific composition. IL-10 is elected with traverse. The allegation on page 3 of the Office Action that the species are distinct because "each of said species has a distinct structure with distinct biochemical properties which are conferred by said distinct structure" is not relevant in this instance. The species all have the common property of being capable of upregulating expression of an endogenous Notch or Notch ligand (see claim 1, for example), and are therefore not distinct.

MPEP 808.01(a) states (in bold print), "[e]lection of species should not be required if the species claimed are considered clearly unpatentable (obvious) over each other."

It is Applicants' understanding that, upon the allowance of a generic claim, Applicants will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include all of the limitations of an allowed generic claim, as provided by 37 C.F.R. 1.141. It is also understood that the Examiner can broaden the search to include other species, e.g., upon determining that a species is allowable, or as discussed herein, when there is a relationship among the species and/or number of species is not too great.

In this regard, M.P.E.P. § 808.01(a) states that "where there is no disclosure of relationship between species (*see* M.P.E.P. §806.04 (b)), they are independent inventions and election of one invention" is required. In view of M.P.E.P. §803, however, when the generic claim includes sufficiently few species that a search and examination of all the species at one time would not impose a serious burden on the examiner, then a requirement for election is inappropriate. Moreover, MPEP 803.02 specifically provides that members of a claimed *Markush* group must be searched and examined together, if they are not too many in number.

Examination of the generic claims, without election, does not impose a serious burden on the Examiner. An examination of claims wherein the cytokine is IL-10, for example, would

inevitably encompass a search that included Il-4, IL-14, and the other recognized members of that group. No election should therefore be required.

The result of the present restriction requirement are inefficiencies and unnecessary expenditures by both the Applicants and the PTO and extreme prejudice to Applicants (particularly in view of GATT, a shortened patent term may result in any divisional applications filed); and restriction has not been shown to be proper, especially since the requisite showing of serious burden has not been made in the Office Action and there are relationships between the claims of all nine Groups. Indeed, the search and examination of each Group is likely to be co-extensive and, in any event, would involve such interrelated art that the search and examination of the entire application can be made without undue burden on the Examiner. All of the preceding, therefore, mitigate against restriction.

In view of the foregoing, reconsideration and withdrawal of the restriction requirement and favorable examination of the pending claims on the merits are respectfully requested.

Respectfully submitted,

FROMMER LAWRENCE & HAUG LLP
Attorneys for Applicants

By: _____

Thomas J. Kowalski
Reg. No. 32,147
Tel (212) 588-0800
Fax (212) 588-0500

VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the Claims:

3. (Amended) A method [according to claim 1] for producing an APC capable of inducing in a T cell tolerance to an allergen or antigen, which method comprises contacting an APC obtained from a human or animal patient with (i) a composition capable of upregulating expression of an endogenous Notch or Notch ligand in the APC and (ii) the allergen or antigen.

4. (Amended) A method [according to claim 1 or claim 2] for producing *ex vivo* a T cell having tolerance to an allergen or antigen which method comprises incubating a T cell obtained from a human or animal patient with an antigen presenting cell (APC) in the presence of (i) a composition capable of upregulating expression of an endogenous Notch or Notch ligand in the APC and/or T cell and (ii) the allergen or antigen.

5. (Amended) The[A] method according to any one of claims 1 to 4, wherein the composition comprises a substance capable of upregulating expression of Notch or a Notch ligand selected from polypeptides and fragments thereof, linear peptides, cyclic peptides, synthetic and natural compounds including low molecular weight organic or inorganic compounds.

6. (Amended) The[A] method according to any one of claims 1 to 4,[5] wherein the composition comprises a polypeptide selected from Noggin, Chordin, Follistatin, Xnr3, FGF and derivatives, fragments, variants and homologues thereof, and immunosuppressive cytokines, or a combination thereof.

8. (Amended) The[A] method according to any one of [the preceding] claims 1 to 4 wherein the Notch ligand is selected from Serrate, Delta and homologues thereof.

9. (Amended) The[A] method according to any one of [the preceding] claims 1 to 4 wherein the APC is a dendritic cell.

10. (Amended) A method for producing a lymphocyte or APC having tolerance to an allergen or antigen which method comprises incubating a lymphocyte or APC obtained from a human or animal patient with a lymphocyte or APC produced by the method of any one of [the preceding] claims 1 to 4.

11. (Amended) A method [according to claim 9] for producing *ex vivo* a T cell having tolerance to an allergen or antigen which method comprises incubating a T cell obtained from a

human or animal patient with a cell produced by the method of any one of [the preceding] claims 1 to 4.

12. (Amended) [Use of a lymphocyte or APC produced by the]A method for[of any one of the preceding claims in] suppressing an immune response in a mammal to an[the] allergen or antigen comprising incubating a lymphocyte or APC obtained from a human or animal patient with (i) a composition capable of upregulating expression of Serrate or Delta in the lymphocyte or APC and (ii) the allergen or antigen and administering the lymphocyte or APC to the mammal.